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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,378	06/19/2006	Ze Li	514572002000	7828

25225 7590 06/09/2008

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EXAMINER	
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ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
06/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,378	LI ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *31-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/13/06; 5/15/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-30, and sequences PBS00024 (SEQ ID NO:210), PBS00040 (SEQ ID NO:225), PBS00044 (SEQ ID NO:229) in the reply filed on February 27, 2008 is acknowledged. The traversal is on the ground(s) that "the lack of unity argument is without merit" and because "the unifying technical feature that distinguishes the invention over prior art is... the combination of sequences complementary to a SARS sequence and sequences complementary to a nucleotide sequence of a non-SARS CoV infectious organism on one biochip for simultaneously detecting SARS and non-SARS infections in the same subject" (p. 3 of remarks). This is not found persuasive because as noted in the previous restriction requirement, Fodor teaches "an oligonucleotide array or chip comprising every 10-mer". This 10-mer array necessarily meets the limitation of the claimed chip, including both a 10-mer with complementarity to a SARS sequence and a 10-mer with complementarity to a non-SARS CoV infectious organism together on the same chip.

The requirement is still deemed proper and is therefore made FINAL.

Claims 31-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 27, 2007.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on March 13, 2006 and May 15, 2007 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-22 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 10/556182 (the ''182 application' herein). Although the conflicting claims are not identical, they are not patentably distinct from each other because while the claims are not identical, the claims of the copending application are directed to obvious variants of the instant claims. The claims of

the instant case and the copending claims are nearly identical. The difference lies in the inclusion of limitations in a different order in the two sets of claims. For example, claim 1 of the copending application is directed to a chip for assaying SARS-CoV which incorporates at least two probes which comprise at least 10 nucleotides complementary to at least two different sequences of SARS-CoV, while the instant claim 1 is directed to a chip for assaying SARS-CoV which incorporates a probe which comprise at least 10 nucleotides complementary to SARS-CoV and one or more other probes which are complementary to a nucleotide sequence of a non-SARS-CoV infectious organism. However, it is noted that these differing limitations between the instant case and the copending '182 application, are in fact present in different claims. In the instant case, claim 2 is directed to at least two oligonucleotides complementary to two different SARS-CoV sequences, as required in claim 1 of the copending application. In the copending application, claim 19 is directed to an oligonucleotide probe complementary to a nucleotide sequence of a coronavirus not related to SARS-CoV, as required in the instant claim 1. The remaining dependent limitations to conserved and variable regions of the SARS-CoV genome are shared almost verbatim between the two copending applications and therefore the claims are obvious over the copending '182 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-7 recite the limitation "the conserved region", "the structural protein", "the non-structural protein", "the variable region" in the body of the claim and the claims depend from claim 2. Claim 2 does not recite anything about a conserved region, a structural protein, a non-structural protein, or a variable region. There is insufficient antecedent basis for this limitation in the claim.

As these limitations are incorporated into claim 5, for purposes of applying art, the claims will be interpreted as depending from claim 5 instead of claim 2.

Claim Objections

Claim 22 is objected to because of the following informalities: "a respiratory sncytical virus" appears to be a typographical error. It is presumed that "a respiratory syncytial virus" was the intended terminology. Appropriate correction is required.

Claim Interpretation

The claims are drawn to a chip comprising oligonucleotide probes that comprise at least 10 nucleotides complementary to a particular nucleotide sequence. Therefore, the claims will be given a broad interpretation based specifically on the "at least 10 nucleotides" limitation. For example, Fodor will be applied broadly over the majority of the claims because the reference

teaches an array comprising all possible 10-mers, which therefore would inherently include those sequences which are specific for SARS-CoV, non-SARS-CoV, etc.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-8, 21 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al. (US Patent 6,355,432; March 2002). Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides).

With regard to claim 1, Fodor teaches a chip for assaying for a coronaviruse causing the severe acute respiratory syndrome (SARS-CoV) and a non-SARS-CoV infectious organism, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon an oligonucleotide probe complementary to a nucleotide sequence of SARS-CoV genome, said nucleotide sequence comprising at least 10 nucleotides, and one or more of the following oligonucleotide probe(s) (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences):

a) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism causing SARS-like symptoms, said nucleotide sequence comprising at least 10 nucleotides (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences);

b) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism damaging an infectious host's immune system, said nucleotide sequence comprising at least 10 nucleotides (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences); or

e) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV coronaviridae virus, said nucleotide sequence comprising at least 10 nucleotides (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 2, Fodor teaches an embodiment of claim 1, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon at least two oligonucleotide probes complementary to at least two different nucleotide sequences of SARS-CoV genome, each of said two different nucleotide sequences comprising at least 10 nucleotides (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 3, Fodor teaches an embodiment of claim 2, wherein the at least two different nucleotide sequences of SARS-CoV genome comprises:

a) a nucleotide sequence of at least 10 nucleotides located within a conserved region of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a variable region of SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences); or

b) a nucleotide sequence of at least 10 nucleotides located within a structural protein coding gene of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a non-structural protein coding gene of SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 4, Fodor teaches an embodiment of claim 2, which further comprises:

a) at least one of the following three oligonucleotide probes: an immobilization control probe that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SAKS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained in the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample (col. 19, lines 42-66, where the process would produce a matrix having each of the

different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences; and also col. 24, lines 15-19, where hybridization controls are included); and b) a blank spot (col. 24, lines 15-19, where hybridization controls are included).

With regard to claim 5, Fodor teaches an embodiment of claim 2, which comprises at least two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides, respectively, located within a conserved region of SARS-CoV genome, located within a structural protein coding gene of SARS-CoV genome or located within a non-structural protein coding gene of SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 6, Fodor teaches an embodiment of claim 2, wherein:
a) the conserved region of S ARS-CoV genome is a region located within the Replicase 1A or 1B gene or the Nucleocapsid (N-) gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences);
b) the structural protein coding gene of SARS-CoV genome is a gene encoding the Spike glycoprotein (S), the small envelope protein (E) or the Nucleocapsid protein (N); or c) the non-structural protein coding gene of SARS-CoV genome is a gene encoding the Replicase 1A or 1B (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 7, Fodor teaches an embodiment of claim 2, wherein the variable region of SARS-CoV genome is a region located within the Spike glycoprotein (S) gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 8, Fodor teaches an embodiment of claim 2, which comprises at least two of the following four oligonucleotide probes: two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides located within the Replicase 1A or 1B gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence of at least 10 nucleotides located within the N gene of SAKS-CoV and an oligonucleotide probe complementary to a nucleotide sequence of at least 10 nucleotides located within the S gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 21, Fodor teaches an embodiment of claim 2, wherein at least one of the oligonucleotide probes is complementary to a highly expressed nucleotide sequence of SARS-CoV genome (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences).

With regard to claim 30, Fodor teaches an embodiment of claim 1, wherein the support comprises a surface that is selected from the group consisting of a silicon, a plastic, a glass, a

ceramic, a rubber, and a polymer surface (col. 36, lines 23-27, where the substrate comprises silicon).

Claims 1-8, 15, 21 and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Rong et al. (Chinese Science Bulletin, June 2003, vol. 48, no. 12, p. 1165-1169) as evidenced by Marra et al. (Science, 2003, vol. 300, p. 1399-1404; epub May 2003). Rong teaches an oligonucleotide microarray in SARS coronavirus detection (Abstract).

With regard to claim 1, Rong teaches a chip for assaying for a coronaviruse causing the severe acute respiratory syndrome (SARS-CoV) and a non-SARS-CoV infectious organism, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon an oligonucleotide probe complementary to a nucleotide sequence of SARS-CoV genome, said nucleotide sequence comprising at least 10 nucleotides, and one or more of the following oligonucleotide probe(s) (p. 1168, col. 2, 'design of the oligos and microarray' heading, Figure 1 and Table 1, where the specific oligonucleotide sequences complementary to SARS-CoV are included):

a) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism causing SARS-like symptoms, said nucleotide sequence comprising at least 10 nucleotides (Table 1, where oligo10 is a sequence that is complementary to multiple non-SARS-CoV organisms, including bovine coronavirus, rat coronavirus and avian infectious bronchitis virus);

b) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism damaging an infectious host's immune system, said nucleotide sequence

comprising at least 10 nucleotides (Table 1, where oligo10 is a sequence that is complementary to multiple non-SARS-CoV organisms, including bovine coronavirus, rat coronavirus and avian infectious bronchitis virus); or

c) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV coronaviridae virus, said nucleotide sequence comprising at least 10 nucleotides (Table 1, where oligo10 is a sequence that is complementary to multiple non-SARS-CoV organisms, including bovine coronavirus, rat coronavirus and avian infectious bronchitis virus).

With regard to claim 2, Rong teaches an embodiment of claim 1, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon at least two oligonucleotide probes complementary to at least two different nucleotide sequences of SARS-CoV genome, each of said two different nucleotide sequences comprising at least 10 nucleotides (p. 1168, col. 2, 'design of the oligos and microarray' heading, Figure 1 and Table 1, where the specific oligonucleotide sequences complementary to SARS-CoV are included).

With regard to claim 3, Rong teaches an embodiment of claim 2, wherein the at least two different nucleotide sequences of SARS-CoV genome comprises:

a) a nucleotide sequence of at least 10 nucleotides located within a conserved region of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a variable region of SARS-CoV genome (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398, which is a conserved region, p. 1401, col. 2); or

b) a nucleotide sequence of at least 10 nucleotides located within a structural protein coding gene of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a non-

structural protein coding gene of SARS-CoV genome (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398, which is a conserved region, p. 1401, col. 2).

With regard to claim 4, Rong teaches an embodiment of claim 2, which further comprises:

a) at least one of the following three oligonucleotide probes: an immobilization control probe that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SAKS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained in the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample (Figure 1, where there were negative control spots included); and

b) a blank spot (Figure 1, where there were empty control spots or blank spots).

With regard to claim 5, Rong teaches an embodiment of claim 2, which comprises at least two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides, respectively, located within a conserved region of SARS-CoV genome, located within a structural protein coding gene of SARS-CoV genome or located within a non-structural protein coding gene of SARS-CoV genome (p. 1168, col. 2, 'design of the oligos and microarray' heading, Figure 1 and Table 1, where the specific oligonucleotide sequences complementary to SARS-CoV are included; Table 1, oligo 2, 16, 12, 9, etc. which are directed to

the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398, which is a conserved region, p. 1401, col. 2).

With regard to claim 6, Rong teaches an embodiment of claim 2, wherein:
a) the conserved region of S ARS-CoV genome is a region located within the Replicase 1A or 1B gene or the Nucleocapsid (N-) gene of SARS-CoV;
b) the structural protein coding gene of SARS-CoV genome is a gene encoding the Spike glycoprotein (S), the small envelope protein (E) or the Nucleocapsid protein (N); or c) the non-structural protein coding gene of SARS-CoV genome is a gene encoding the Replicase 1A or 1B (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398, which is a conserved region, p. 1401, col. 2).

With regard to claim 7, Rong teaches an embodiment of claim 2, wherein the variable region of SARS-CoV genome is a region located within the Spike glycoprotein (S) gene of SARS-CoV (Table 1, oligo 28 and oligo 05, which are directed to spike glycoprotein, as evidenced by Marra et al., Figure 1, where the Spike glycoprotein falls between 21,492-25,259).

With regard to claim 8, Rong teaches an embodiment of claim 2, which comprises at least two of the following four oligonucleotide probes: two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides located within the Replicase 1A or 1B gene of SARS-CoV (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398), an oligonucleotide probe complementary to a nucleotide sequence of at least 10 nucleotides located within the N gene of SAKS-CoV and an oligonucleotide probe

complementary to a nucleotide sequence of at least 10 nucleotides located within the S gene of SARS-CoV (Table 1, oligo 28 and oligo 05, which are directed to spike glycoprotein, as evidenced by Marra et al., Figure 1, where the Spike glycoprotein falls between 21,492-25,259).

With regard to claim 15, Rong teaches an embodiment of claim 4, wherein the label of the immobilization control probe is selected from the group consisting of a chemical, an enzymatic, an immunogenic, a radioactive, a fluorescent, a luminescent and a FRET label (p. 1166, col. 2, where the cDNAs were fluorescently labeled).

With regard to claim 21, Rong teaches an embodiment of claim 2, wherein at least one of the oligonucleotide probes is complementary to a highly expressed nucleotide sequence of SARS-CoV genome (p. 1168, col. 2, 'design of the oligos and microarray' heading, Figure 1 and Table 1, where the specific oligonucleotide sequences complementary to SARS-CoV are included).

With regard to claim 29, Rong teaches an embodiment of claim 1, wherein the non-SARS-CoV coronaviridae virus is selected from the group consisting of an avian infectious bronchitis virus, an avian infectious laryngotracheitis virus, a murine hepatitis virus, an equine coronaviruse, a canine coronaviruse, a feline coronaviruse, a porcine epidemic diarrhea virus, a porcine transmissible gastroenteritis virus, a bovine coronaviruse, a feline infectious peritonitis virus, a rat coronaviruse, a neonatal calf diarrhea coronavimse, a porcine hemagglutinating encephalomyelitis virus, a puffimosis virus, a turkey coronaviruse and a sialodacryoadenitis virus of rat (Table 1, where oligo10 is a sequence that is complementary to multiple non-SARS-CoV organisms, including bovine coronavirus, rat coronavirus and avian infectious bronchitis virus).

With regard to claim 30, Rong teaches an embodiment of claim 1, wherein the support comprises a surface that is selected from the group consisting of a silicon, a plastic, a glass, a ceramic, a rubber, and a polymer surface (p. 1168, col. 1, 'preparation of the 60-mer oligonucleotide microarray heading' where silanized slides were coated with poly lysine prior to the addition of oligonucleotide probes).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Ruan et al. (2003, The Lancet, 361(9371): 1779-85).

While Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides), Fodor does not explicitly teach the sequence of SEQ ID NO:229 below.

With regard to claim 9, Ruan teaches an embodiment of claim 8, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a Replicase 1A or 1B nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:210 (see alignment below, between SEQ ID NO:210 and AY283798); or

```
Query  1     TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT  60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  9256  TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT
9315

Query  61    CAGTAGTGGC  70
             ||||||||||
Sbjct  9316  CAGTAGTGGC  9325
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b) has at least 90% identity to a Replicase 1A or 1B nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

With regard to claim 10, Ruan teaches an embodiment of claim 9, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Briese et al. (US PgPub 20040265796; December 2004, 102(e) date April 17, 2003).

While Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides), Fodor does not explicitly teach the sequence of SEQ ID NO:229 below.

With regard to claim 11, Briese teaches an embodiment of claim 8, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence

that:

a) hybridizes, under high stringency, with a N nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:225 (see alignment below between SEQ ID NO:1 of Briese and with SEQ ID NO:225); or

```
Qy          1 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        255 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA
314

Qy         61 AAGTTTCTGG 70
              ||||||||||
Db        315 AAGTTTCTGG 324
```

b) has at least 90% identity to a N nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

With regard to claim 12, Briese teaches an embodiment of claim 11, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary

skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Vilalta et al. (WO2005021707; March 2005; with priority to 60/470820, effective date May 16, 2003).

While Fodor teaches an oligonucleotide array or chip comprising every possible 10-mer (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides), Fodor does not explicitly teach the sequence of SEQ ID NO:229 below.

With regard to claim 13, Vilalta teaches an embodiment of claim 8, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a S nucleotide sequence, or a complementary strand thereof, that is set forth in SEQ ID NO:229 (see alignment below between SEQ ID NO:3 of Vilalta); or

```
Qy          1 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1754 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG 1813

Qy         61 ATGTTTCTAC 70
              ||||||||||
Db       1814 ATGTTTCTAC 1823
```

b) has at least 90% identity to a S nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

With regard to claim 14, Vilalta teaches an embodiment of claim 13, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Martoglio et al. (Molecular Medicine, 2000, 6(9):750-765).

With regard to claim 18, Fodor teaches an embodiment of claim 8, which comprises two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences), an immobilization control probe that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SARS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained in the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences; also col. 24, lines 15-19, where hybridization controls are included).

With regard to claim 19, Fodor teaches an embodiment of claim 18, which comprises multiple spots of the two oligonucleotide probes complementary to two different nucleotide

sequences located within the Replicase 1B gene of SAKS-CoV, the oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV, the oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV (col. 19, lines 42-66, where the process would produce a matrix having each of the different possible 10-mer oligonucleotides and therefore would inherently include each of these sequences), the immobilization control probe, the positive control probe and the negative control probe (col. 24, lines 15-19, where hybridization controls are included).

Regarding claims 16-17, Fodor does not teach the spiking of a non-SARS-CoV sequence in the sample and also does not teach that the sequence is of Arabidopsis origin. Regarding claims 18 and 19, Fodor does not teach the inclusion of an immobilization control probe or a positive control probe. Martoglio teaches the inclusion of these probes in a microarray format.

With regard to claim 16-17, Martoglio teaches spiking a non-SARS-CoV sequence in the sample to be assayed and that the sequence is of Arabidopsis origin (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, 'processing hybridization signals' heading).

With regard to claim 18-19, Martoglio teaches an immobilization control probe and a positive control probe (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, 'processing hybridization signals' heading).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Fodor to arrive at the claimed

invention with a reasonable expectation for success. As taught by Martoglio, "To account for potential differences in probe labeling, each data set was normalized with respect to the corresponding mean signal intensity of *Arabidopsis thaliana* cytochrome c554 cDNA added to each probe as direct internal controls, as described above" (p. 753, 'processing hybridization signals' heading). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Fodor to arrive at the claimed invention with a reasonable expectation for success.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Saiki et al. (PNAS, 1989, vol. 86, p. 6230-6234).

With regard to claim 20, Saiki teaches an embodiment of claim 4, wherein at least one of the oligonucleotide probe comprises, at its 5' end, a poly dT region to enhance its immobilization on the support (p. 6230, 'tailing of oligonucleotides' heading, where the oligos were tailed with poly dT prior to immobilization).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the teachings of tailed oligonucleotides to the 10-mer array or chip of Fodor to arrive at the claimed invention with a reasonable expectation for success. As taught by Saiki, "in a single hybridization reaction, an entire series of sequences could be examined simultaneously". Saiki also teaches "the poly(dT) tail would be a larger target for UV crosslinking and should preferentially react with the nylon" (p. 6230, col. 1).

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have incorporated the teachings of tailed oligonucleotides to the 10-mer array or chip of Fodor to arrive at the claimed invention with a reasonable expectation for success.

Claims 22-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor as applied to claims 1-8, 21 and 30 above and further in view of Marra et al. (Science, 2003, vol. 300, p. 1399-1404; epub May 2003).

With regard to claim 22-23, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism causing SARS-like symptoms is selected from the group consisting of a human coronaviruse 229E, a human coronaviruse 0C43, a human enteric coronaviruse, an influenza virus, a parainfluenza virus, a respiratory sncytical virus, a human metapneumovirus, a rhinovirus, an adenoviruse, a mycoplasma pneumoniae, a chlamydia pneumoniae, a measles virus and a rubella virus (Figure 1, legend, where human coronavirus was included in the listing).

With regard to claim 24, Marra teaches an embodiment of claim 22, wherein the parainfluenza virus is selected from the group consisting of parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3 and parainfluenza virus 4 (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 25, 27, 28, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism damaging an infectious host's immune system is selected from the group consisting of a hepatitis virus, a transfusion transmitting virus (TTV), a human immunodeficiency virus (HIV), a parvovirus, a human cytomegalovirus (HCMV), an Epstein-

Barr virus (EBV) and a tre-ponema palidum (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 26, Marra teaches an embodiment of claim 25, wherein the hepatitis virus is selected from the group consisting of hepatitis virus A (HAV), hepatitis virus B (HBV), hepatitis virus C (HCV), hepatitis virus D (HDV), hepatitis virus E (HEV) and hepatitis virus G (HGV) (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 29, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV coronaviridae virus is selected from the group consisting of an avian infectious bronchitis virus, an avian infectious laryngotracheitis virus, a murine hepatitis virus, an equine coronaviruse, a canine coronaviruse, a feline coronaviruse, a porcine epidemic diarrhea virus, a porcine transmissible gastroenteritis virus, a bovine coronaviruse, a feline infectious peritonitis virus, a rat coronaviruse, a neonatal calf diarrhea coronavimse, a porcine hemagglutinating encephalomyelitis virus, a puffimosis virus, a turkey coronaviruse and a sialodaeryoadenitis virus of rat (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Rong to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success. While Marra does not teach the inclusion of these various non-SARS-CoV organisms in a microarray format, Marra does establish the phylogenetic relationship between the SARS-CoV genome, and particular coding features within the genome

as compared to these non-SARS-CoV sequences. As Rong already includes a probe complementary to a non-SARS-CoV sequence, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Rong to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success.

Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rong as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Ruan et al. (2003, The Lancet, 361(9371): 1779-85).

While Rong teaches probes that hybridize with the SARS-CoV genome, Rong does not teach the specific sequence as claimed below.

With regard to claim 9, Ruan teaches an embodiment of claim 8, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a Replicase 1A or 1B nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:210 (see alignment below, between SEQ ID NO:210 and AY283798); or

```
Query  1     TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT  60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  9256  TCATAGCTAACATCTTTACTCCTCTTGTGCAACCTGTGGGTGCTTTAGATGTGTCTGCTT
9315

Query  61    CAGTAGTGGC  70
             ||||||||||
Sbjct  9316  CAGTAGTGGC  9325
```

b) has at least 90% identity to a Replicase 1A or 1B nucleotide sequence comprising a nucleotide

sequence, or a complementary strand thereof, that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

With regard to claim 10, Ruan teaches an embodiment of claim 9, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:210 (see alignment above, between SEQ ID NO:210 and AY283798).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rong as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Briese et al. (US PgPub 20040265796; December 2004, 102(e) date April 17, 2003).

While Rong teaches probes that hybridize with the SARS-CoV genome, Rong does not teach the specific sequence as claimed below.

With regard to claim 11, Briese teaches an embodiment of claim 8, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a N nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:225 (see alignment below between SEQ ID NO:1 of Briese and with SEQ ID NO:225); or

```
Qy          1 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        255 GAGGTGGTGAAACTGCCCTCGCGCTATTGCTGCTAGACAGATTGAACCAGCTTGAGAGCA 314

Qy         61 AAGTTTCTGG 70
              ||||||||||
Db        315 AAGTTTCTGG 324
```

b) has at least 90% identity to a N nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

With regard to claim 12, Briese teaches an embodiment of claim 11, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:225 (see alignment above between SEQ ID NO:1 of Briese and with SEQ ID NO:225).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rong as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Vilalta et al. (WO2005021707; March 2005; with priority to 60/470820, effective date May 16, 2003).

While Rong teaches probes that hybridize with the SARS-CoV genome, Rong does not teach the specific sequence as claimed below.

With regard to claim 13, Vilalta teaches an embodiment of claim 8, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a S nucleotide sequence, or a complementary strand thereof, that is set forth in SEQ ID NO:229 (see alignment below between SEQ ID NO:3 of Vilalta); or

```
Qy          1 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1754 CACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTG 1813

Qy         61 ATGTTTCTAC 70
              ||||||||||
Db       1814 ATGTTTCTAC 1823
```

b) has at least 90% identity to a S nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

With regard to claim 14, Vilalta teaches an embodiment of claim 13, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that is SEQ ID NO:229 (see alignment above between SEQ ID NO:3 of Vilalta).

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers and probes for the detection of SARS-CoV, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rong as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Martoglio et al. (Molecular Medicine, 2000, 6(9):750-765).

With regard to claim 18, Rong teaches an embodiment of claim 8, which comprises two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398), an oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV (Table 1, oligo 27 and oligo 18, which are directed to the nucleocapsid or N gene, as evidenced by Marra, et al., Figure 1, where the N gene falls between 28,120-29,388), an oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV, a negative control probe that is not complementary to any nucleotide sequence contained in the sample (Figure 1, where there were negative control spots included and where there were empty control spots or blank spots).

With regard to claim 19, Rong teaches an embodiment of claim 18, which comprises multiple spots of the two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV (Table 1, oligo 2, 16, 12, 9, etc. which are directed to the replicase 1A sequence, as evidenced by Marra et al, Figure 1, where the replicase 1A sequence falls between 265-13,398), the oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV (Table 1, oligo 27 and oligo 18, which are directed to the nucleocapsid or N gene, as evidenced by Marra, et al., Figure 1, where the N gene falls between 28,120-29,388), the oligonucleotide probe

complementary to a nucleotide sequence located within the S gene of SARS-CoV (Table 1, oligo 28 and oligo 05, which are directed to spike glycoprotein, as evidenced by Marra et al., Figure 1, where the Spike glycoprotein falls between 21,492-25,259), and the negative control probe (Figure 1, where there were negative control spots included and where there were empty control spots or blank spots).

Regarding claims 16-17, Rong does not teach the spiking of a non-SARS-CoV sequence in the sample and also does not teach that the sequence is of Arabidopsis origin. Regarding claims 18 and 19, Rong does not teach the inclusion of an immobilization control probe or a positive control probe. Martoglio teaches the inclusion of these probes in a microarray format.

With regard to claim 16-17, Martloglio teaches spiking a non-SARS-CoV sequence in the sample to be assayed and that the sequence is of Arabidopsis origin (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, 'processing hybridization signals' heading).

With regard to claim 18-19, Martoglio teaches an immobilization control probe and a positive control probe (p. 752, col. 1-2, where the samples were spiked with an Arabidopsis cytochrome cDNA as a control for labeling and hybridization; see also p. 753, 'processing hybridization signals' heading).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Rong to arrive at the claimed invention with a reasonable expectation for success. As taught by Martoglio, "To account for potential differences in probe labeling, each data set was normalized with respect to the

corresponding mean signal intensity of *Arabidopsis thaliana* cytochrome c554 cDNA added to each probe as direct internal controls, as described above" (p. 753, 'processing hybridization signals' heading). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have included the additional controls for microarray normalization taught by Martoglio to the array for SARS-CoV sequences taught by Rong to arrive at the claimed invention with a reasonable expectation for success.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rong as applied to claims 1-8, 21 and 29-30 above and further in view of Saiki et al. (PNAS, 1989, vol. 86, p. 6230-6234).

With regard to claim 20, Saiki teaches an embodiment of claim 4, wherein at least one of the oligonucleotide probe comprises, at its 5' end, a poly dT region to enhance its immobilization on the support (p. 6230, 'tailing of oligonucleotides' heading, where the oligos were tailed with poly dT prior to immobilization).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the teachings of tailed oligonucleotides to the 10-mer array or chip of Fodor to arrive at the claimed invention with a reasonable expectation for success. As taught by Saiki, "in a single hybridization reaction, an entire series of sequences could be examined simultaneously". Saiki also teaches "the poly(dT) tail would be a larger target for UV crosslinking and should preferentially react with the nylon" (p. 6230, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have been

motivated to have incorporated the teachings of tailed oligonucleotides to the 10-mer array or chip of Fodor to arrive at the claimed invention with a reasonable expectation for success.

Claims 22-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rong as applied to claims 1-8, 15, 21 and 29-30 above and further in view of Marra et al. (Science, 2003, vol. 300, p. 1399-1404; epub May 2003).

With regard to claim 22-23, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism causing SARS-like symptoms is selected from the group consisting of a human coronaviruse 229E, a human coronaviruse 0C43, a human enteric coronaviruse, an influenza virus, a parainfluenza virus, a respiratory sncytical virus, a human metapneumovirus, a rhinovirus, an adenoviruse, a mycoplasma pneumoniae, a chlamydia pneumoniae, a measles virus and a rubella virus (Figure 1, legend, where human coronavirus was included in the listing).

With regard to claim 24, Marra teaches an embodiment of claim 22, wherein the parainfluenza virus is selected from the group consisting of parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3 and parainfluenza virus 4 (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 25, 27, 28, Marra teaches an embodiment of claim 1, wherein the non-SARS-CoV infectious organism damaging an infectious host's immune system is selected from the group consisting of a hepatitis virus, a transfusion transmitting virus (TTV), a human immunodeficieney virus (HIV), a parvovirus, a human cytomegalovirus (HCMV), an Epstein-

Barr virus (EBV) and a tre-ponema palidum (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

With regard to claim 26, Marra teaches an embodiment of claim 25, wherein the hepatitis virus is selected from the group consisting of hepatitis virus A (HAV), hepatitis virus B (HBV), hepatitis virus C (HCV), hepatitis virus D (HDV), hepatitis virus E (HEV) and hepatitis virus G (HGV) (Figure 1, legend, where a variety of additional viruses and organisms are listed as related to SARS-CoV phylogenetically).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Rong to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success. While Marra does not teach the inclusion of these various non-SARS-CoV organisms in a microarray format, Marra does establish the phylogenetic relationship between the SARS-CoV genome, and particular coding features within the genome as compared to these non-SARS-CoV sequences. As Rong already includes a probe complementary to a non-SARS-CoV sequence, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Rong to include the additional non-SARS-CoV infectious organisms disclosed by Marra to arrive at the claimed invention with a reasonable expectation for success.

Relevant Prior art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Affymetrix Press release (May 6, 2003, pages 1-2) discloses a new GeneChip™ CustomSeq™ SARS Pathogen detection and resequencing array (p. 1).

Conclusion

All claims stand rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Stephanie K. Mummert/
Patent Examiner, Art Unit 1637

SKM